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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/609,383	07/03/2000	Dirk Heinegard	06803.0008	3999

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EXAMINER

HUYNH, PHUONG N

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 04/23/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/609,383

Applicant(s)

HEINEGARD ET AL.

Examiner

" Neon" Phuong Huynh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE Three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,18 and 36-56 is/are pending in the application.
- 4a) Of the above claim(s) 18 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 49,50 and 56 is/are allowed.
- 6) ☒ Claim(s) 1,3-6,36-48 and 51-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 3-6, 18 and 36-56 are pending.
2. Claim 18 stands withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.
3. The drawings, filed 2/8/02, are approved.
4. The declaration filed by D Heinegard on 1/30/02 has overcome the rejection under 35 U.S.C. 102(a) as being anticipated by Lorenzo *et al* (J Bio Chem 273(36): 23469-75, Sept 1998; PTO 1449).
5. The following new grounds of rejections are necessitated by the amendment filed 1/30/02.
6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
 7. The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
8. Claims 1, 3-6, 36-48 and 51-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a purified or isolated human peptide of SEQ ID NO: 2 wherein the peptide is a human cartilage intermediate layer protein (CILP) and fragments of a human CILP selected from the group consisting of SEQ ID NO: 3-17 and 21-22 for making antibody (pages 27 and 49) and for detection assay (page 30), **does not** reasonably provide enablement for a purified or isolated peptide wherein the peptide is (1) *any* cartilage intermediate layer protein (CILP) "comprising" residues 1-682 of SEQ ID NO: 2, (2) *any* "analog" of a CILP "comprising" residues 1-682 of SEQ ID NO: 2, (3) *any* fragment of *any* CILP wherein the fragment is immunoreactive with at least one antibody that is specific for a CILP "comprising" residues 1-682 of SEQ ID NO: 2, (4) *any* cartilage intermediate layer protein (CILP) "comprising" residues 1-682 of SEQ ID NO: 2 wherein said peptide is expressed in early osteoarthritis, (5) *any* "analog" of a CILP "comprising" residues 1-682 of SEQ ID NO: 2 wherein said peptide is expressed in early osteoarthritis, (6) *any* fragment of *any* CILP wherein said

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peptide is expressed in early osteoarthritis, (7) *any* fragment of *any* analog of a CILP wherein said peptide is expressed in early osteoarthritis, (8) *any* peptide, analog, fragment mentioned above wherein said peptide is a human peptide, (9) *any* CILP that is expressed in early osteoarthritis, wherein said CILP “comprises” *any* amino acid sequence that shows “at least 50% amino acid identity” to residues 1-682 of SEQ ID NO: 2 and is immunoreactive with at least one antibody that is raised against a CILP encoded by SEQ ID NO: 1, *any* CILP that is expressed in early osteoarthritis, wherein said CILP comprises *any* amino acid sequence that shows (10) “at least 60% amino acid identity” to residues 1-682 of SEQ ID NO: 2, (11) “at least 70% amino acid identity” to residues 1-682 of SEQ ID NO: 2, (12) “at least 80% amino acid identity” to residues 1-682 of SEQ ID NO: 2, (13) “at least 90% amino acid identity” to residues 1-682 of SEQ ID NO: 2, (14) “at least 95% amino acid identity” to residues 1-682 of SEQ ID NO: 2, (12) “at least 99% amino acid identity”, to residues 1-682 of SEQ ID NO: 2, (15) *any* isolated or purified wherein said CILP “comprises” residues 1-682 of SEQ ID NO: 2 and has a molecular mass of 92,000 when expressed in cells, (16) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 90% identity to residues 1-682 of SEQ ID NO: 2 wherein said human CILP has a molecular mass of 78,500, (17) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 95% identity to residues 1-682 of SEQ ID NO: 2, (18) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 99% identity to residues 1-682 of SEQ ID NO: 2 for making antibody and detection assay. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants’ arguments filed 1/30/02 have been fully considered but are not found persuasive.

Applicants’ position is that claims 2, 7, 8, 23, 24 and 35 are canceled by this amendment.

However, the amended claim 1 introduces new problem because of the recitation of “comprising” for a specific fragment of SEQ ID NO: 2. Further, the amendment has not address the issues of analog of CILP, and fragment of analog of CILP. Without the specific SEQ ID NO, there is no structure associated with functions associated with “analog”, and “fragment” thereof.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope

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of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a purified or isolated human peptide of SEQ ID NO: 2 wherein the peptide is a cartilage intermediate layer protein (CILP) and fragments of a human CILP selected from the group consisting of SEQ ID NO: 3-17 and 21-22 for making antibody for detection assays.

The specification does not teach how to make and use *any* cartilage intermediate layer protein (CILP) “comprising” residues 1-682 of SEQ ID NO: 2 because residues 1-682 of SEQ ID NO: 2 is a fragment of SEQ ID NO: 2. The term “comprising” is open-ended. It expands the fragment to include additional amino acid residues at either end. As such, the length of the fragment could expand to infinity. Given the indefinite number of undisclosed amino acid residues, it is unpredictable which undisclosed fragment will have the same structure and functions as SEQ ID NO: 2, in turn, for generating antibody that would be specific for cartilage intermediate layer protein. Further, there is insufficient guidance and working examples in the specification as how to make and use any purified or isolated peptide wherein the peptide is *any* “analog” of a CILP “comprising” residues 1-682 of SEQ ID NO: 2, any fragment of *any* CILP, any CILP analog wherein said “analog” of a CILP, “fragment” of CILP, CILP analog would react with at least one antibody that is specific for CILP or CILP analog “comprising” residues 1-682 of SEQ ID NO: 2. Since the specific amino acid residues of CILP “comprising” residues 1-682 of SEQ ID NO: 2 is not enable, it follows that *any* analog of CILP comprising residues 1-682 of SEQ ID NO: 2, *any* fragment of said undisclosed CILP, *any* fragment of said undisclosed CILP analog is not enabled.

Other than the specific human CILP peptide and fragments consisting of SEQ ID NO: 3-17 and 21-22 mentioned above for antibody production and detection assay, the specification fails to provide any guidance as how to make and use *any* purified or isolated peptide wherein the peptide is any cartilage intermediate layer protein (CILP) comprising residues 1-682 of SEQ ID NO: 2, *any* analog of *any* CILP comprising residues 1-682 of SEQ ID NO: 2, *any* fragment of any CILP, *any* fragment of *any* CILP analog wherein said analog, CILP comprising residues 1-682 of SEQ ID NO: 2, and fragment thereof that would immunoreactive with an antibody that is specific

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for a CILP “comprising” residues 1-682 of SEQ ID NO: 2, or any CILP analog “comprising” residues 1-682 of SEQ ID NO: 2 with any specificity. Given that the peptide is not enabled, it follows that the antibody generated from said peptide is not enabled.

Ngo *et al* (of record) teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo *et al.*, 1994, *The Protein Folding Problem and Tertiary Structure Prediction*, pp. 492-495). Given the lack of guidance and working examples, predicting what changes can be made to the amino acid sequence of a CILP comprising 1-682 residues of SEQ ID NOS: 2 that after substitution, deletion, insertion and/or modification will retain both structure and have similar function is unpredictable. It follows that any analog, and fragment thereof are not enabled.

With regard to CILP “comprises” an amino acid sequence that shows “at least 50% identity” to residues 1-682 of SEQ ID NO: 2, there is at least a 50% difference in the amino acid residues 1-682 of SEQ ID NO: 2, which amounts to at least 341 amino acids difference. Further, the term “comprises” is open-ended. It expands the undisclosed CILP to include additional amino acid residues at either end to read on infinity, in addition to CILP that has 341 amino acids difference. Given the lack of guidance as to which specific amino acid within SEQ ID NO: 2 can tolerate change, and the insufficient working example, it is unpredictable as to which undisclosed CILP that minimally has 341 amino acids difference from residues 1-682 of SEQ ID NO: 2 would even bind to an antibody that is raised against a CILP encoded by SEQ ID NO: 1. Even if there is a 1% difference in the amino acid residues 1-682 of SEQ ID NO: 2, there is a minimum of about 7 amino acids difference.

Abaza *et al* teach that even one amino acid difference outside of an antigenic site of a protein, there is a complete loss of reactivity with two antibodies that is specific for the protein (See abstract, in particular). Given the lack of guidance as to which specific amino acid residue of SEQ ID NO: 2 can tolerate change and the insufficient working examples in the specification as filed, further research is required.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention without undue amount of experimentation.

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9. Claims 1, 3-6, 36-48 and 51-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed 1/30/02 have been fully considered but are not found persuasive.

Applicants' position is that claims 2, 7, 8, 23, 24 and 35 are canceled by this amendment.

However, the amended claim 1 introduces new problem because of the recitation of "comprising" for a specific fragment of SEQ ID NO: 2. Further, the amendment has not address the issues of analog of CILP, and fragment of analog of CILP. Without the specific SEQ ID NO, there is no structure associated with functions associated with analog, and fragment thereof.

The specification does not reasonably provide a **written description** of (1) *any* cartilage intermediate layer protein (CILP) "comprising" residues 1-682 of SEQ ID NO: 2, (2) *any* "analog" of a CILP "comprising" residues 1-682 of SEQ ID NO: 2, (3) *any* fragment of *any* CILP wherein the fragment is immunoreactive with at least one antibody that is specific for a CILP "comprising" residues 1-682 of SEQ ID NO: 2, (4) *any* cartilage intermediate layer protein (CILP) "comprising" residues 1-682 of SEQ ID NO: 2 wherein said peptide is expressed in early osteoarthritis, (5) *any* "analog" of a CILP "comprising" residues 1-682 of SEQ ID NO: 2 wherein said peptide is expressed in early osteoarthritis, (6) *any* fragment of *any* CILP wherein said peptide is expressed in early osteoarthritis, (7) *any* fragment of *any* analog of a CILP wherein said peptide is expressed in early osteoarthritis, (8) *any* peptide, analog, fragment mentioned above wherein said peptide is a human peptide, (9) *any* CILP that is expressed in early osteoarthritis, wherein said CILP "comprises" *any* amino acid sequence that shows "at least 50% amino acid identity" to residues 1-682 of SEQ ID NO: 2 and is immunoreactive with at least one antibody that is raised against a CILP encoded by SEQ ID NO: 1, *any* CILP that is expressed in early osteoarthritis, wherein said CILP comprises any amino acid sequence that shows (10) "at least 60% amino acid identity" to residues 1-682 of SEQ ID NO: 2, (11) "at least 70% amino acid identity" to residues 1-682 of SEQ ID NO: 2, (12) "at least 80% amino acid identity" to residues 1-682 of SEQ ID NO: 2, (13) "at least 90% amino acid identity" to residues 1-682 of SEQ ID NO: 2, (14) "at least 95% amino acid identity" to residues 1-682 of SEQ ID NO: 2, (12) "at least 99% amino acid identity", to residues 1-682 of SEQ ID NO: 2, (15) *any* isolated or purified wherein said CILP "comprises" residues 1-682 of SEQ ID NO: 2 and has a molecular mass of

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92,000 when expressed in cells, (16) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 90% identity to residues 1-682 of SEQ ID NO: 2 wherein said human CILP has a molecular mass of 78,500, (17) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 95% identity to residues 1-682 of SEQ ID NO: 2, (18) *any* isolated or purified human CILP “comprises” *any* amino acid sequence that shows “at least 99% identity to residues 1-682 of SEQ ID NO: 2 for antibody detection assay.

The specification discloses only a purified or isolated human peptide of SEQ ID NO: 2 wherein the peptide is a cartilage intermediate layer protein (CILP) and fragments of a human CILP selected from the group consisting of SEQ ID NO: 3-17 and 21-22.

With the exception of the specific human CILP peptide of SEQ ID NO: 2 and fragments of human CILP peptides “consisting” of SEQ ID NO: 3-17 and 21-22, there is insufficient written description about the structure associated with functions of (1) *any* cartilage intermediate layer protein (CILP) “comprising” residues 1-682 of SEQ ID NO: 2, (2) *any* “analog” of a CILP “comprising” residues 1-682 of SEQ ID NO: 2, (3) *any* fragment of *any* CILP wherein the fragment is immunoreactive with at least one antibody that is specific for a CILP “comprising” residues 1-682 of SEQ ID NO: 2, (4) *any* “analog” of a CILP and fragment thereof “comprising” residues 1-682 of SEQ ID NO: 2, (5) *any* CILP that is expressed in early osteoarthritis, wherein said CILP “comprises” *any* amino acid sequence that shows “at least 50%, 60%, 70%, 80%, 90%, 95% or 99%” amino acid identity to residues 1-682 of SEQ ID NO: 2 mentioned above. Further, applicant discloses only CILP from human, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398. Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 “Written Description” Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

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has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

11. Claims 1, 4-6 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Masuda *et al* (of record, Gene 197: 277-287, Sept 1997; PTO 892).

Masuda *et al* teach a purified or isolated porcine NTPPHase protein or recombinant peptide from porcine chondrocyte, which is an analog of a cartilage intermediate layer protein (CILP) (See page 282, reference sequence, in particular). The reference protein has 599 amino acids (See page 281, column 1, last paragraph, in particular) which is a carboxyl-terminal fragment of NTPPHase (See page 285, column 2 line 1-2, in particular) and the reference fragment is immunoreactive with at least one antibody that is specific for a CILP (See page 285 and Fig 5B of Gene 197: 277-287, in particular) and as disclosed on page 51, lines 2-4 and page 42 line 12-15 of instant specification. Claim 36 is included in this rejection because expression of the reference protein is inherent properties of the reference peptide. Thus, the reference teachings anticipate the claimed invention.

12. Claims 1, 3-6, 36-48 and 51-52 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 5,876,963 (of record, March 1999; PTO 892).

The '963 patent teaches a purified or isolated polypeptide (peptide) of human (which is a mammal) pyrophosphohydrolase-1 (NTPPH-1) wherein the polypeptide is an analog of a cartilage intermediate layer protein (CILP) and the reference polypeptide is a fragment of the claimed peptide which has 99.7% identity to the claimed peptide of SEQ ID NO: 2 (See Figs 1A-H, SEQ ID NO: 1 of '963, column 9, lines 40-61, in particular). The term comprising is open-ended. It expands the claimed peptide to read on the reference peptide. The reference peptide is isolated from human articular cartilage (See column 9 line 60-61, in particular). The '963 patent further teaches the method of making the reference polypeptide or fragments thereof using the reference polynucleotide recombinantly (See column 12, lines 16-55, column 17 lines 8-43, in particular). Claim 36 is included in this rejection because expression of the reference protein is inherent properties of the reference peptide. Claims 38-44 and 48 are included in this rejection because the reference peptide has 99.7% identity which is at least 50%, 60%, 70%, 80%, 90%, 95% and 99% identity to the claimed peptide "comprises" an amino acid sequence SEQ ID NO: 2. Claims 45 and 46 are included in this rejection because molecular mass is an inherent property of the reference peptide. Claim 51 and 52 are included in this rejection because the reference

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peptide would inherently bind to the antibody raised against CILP encoded by SEQ ID NO: 1. Since the Patent Office does not have the facilities for examining and comparing the antibody raised against a CILP encoded by SEQ ID NO: 1 would bind to the reference peptides of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

13. Claims 1, 3-6, 36-48 and 51-52 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 6,124,095 (filed Dec 1997; PTO 892).

The '095 patent teaches a purified or isolated polypeptide (peptide) such as pyrophosphohydrolase-2 (NTPPH-2) from human wherein the polypeptide is an analog of a cartilage intermediate layer protein (CILP) and the reference polypeptide is a fragment which has 99.7% identity to the claimed peptide of SEQ ID NO: 2 (See Figs 2A-C, SEQ ID NO: 3 of '095, in particular). The term comprising is open-ended. It expands the claimed peptide to read on the reference peptide. The reference polypeptide is isolated from human osteoarthritic synovial chondrocyte (See column 11 line 26-27, in particular). The '095 patent further teaches the method of making the reference polypeptide or fragments thereof using the reference polynucleotide recombinantly (See column 14, lines 59-67, in particular). Claim 36 is included in this rejection because expression of the reference protein is inherent properties of the reference peptide. Claims 38-44 and 48 are included in this rejection because the reference peptide has 99.7% identity which is at least 50%, 60%, 70%, 80%, 90%, 95% and 99% identity to the claimed peptide "comprises" an amino acid sequence SEQ ID NO: 2. Claims 45 and 46 are included in this rejection because molecular mass is an inherent property of the reference peptide. Claim 51 and 52 are included in this rejection because the reference peptide would inherently bind to the antibody raised against CILP encoded by SEQ ID NO: 1. Since the Patent Office does not have the facilities for examining and comparing the antibody raised against a CILP encoded by SEQ ID NO: 1 would bind to the reference peptides of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Thus, the reference teachings anticipate the claimed invention.

14. Claims 49-50 and 56 are allowed.

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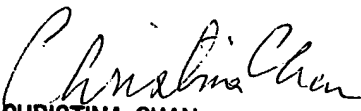
15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
April 22, 2002


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600